

Remarks

Support for the Amendments

Support for the amendments to claims 52, 57-59, 61-65, 69-72, 74-76 and 78 can be found throughout the present specification. Specifically, support for the amendments to the claims can be found throughout pages 31-46 and throughout the Examples and Figures. Therefore, these amendments do not add new matter and their entry and consideration are respectfully requested.

Status of the Claims

By the foregoing amendments, claims 52, 57-59, 61-65, 69-72, 74-76 and 78 are sought to be amended. Upon entry of the foregoing amendments, claims 52-59 and 61-78 are pending in the application, with claims 52, 69, 71 and 75 being the independent claims.

Summary of the Office Action

In the Office Action dated April 20, 2005, the Examiner has made two rejections of, and one objection to, the claims. Based on the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding rejections and objections and that they be withdrawn.

The Rejection Under 35 U.S.C. § 102(b) Over Bebee

In the Office Action at pages 2-6, the Examiner has rejected claims 52-59, 61-63 and 66-78 under 35 U.S.C. § 102 (b), as being anticipated by Bebee *et al.*, U.S. Patent No. 5,434,066 (hereinafter "Bebee"). Applicants respectfully traverse this rejection.

The Examiner states that Bebee discloses the generation of several different vectors using sequences obtained from the phage P1 genome. The Examiner states, with regard to Example 3:

[i]n this example, the "recombination protein" is the ligase used to join a linear fragment of DNA comprising adapters at either terminus that in turn comprise "at least a portion of" a recombination site (e.g., *any* dinucleotide sequence found in *any* given recombination site) with a vector nucleic acid in an *in vitro* reaction mixture.

Office Action at page 4, second paragraph, lines 5-8 (emphasis in original). The Examiner therefore concludes that Bebee discloses the presently claimed invention. Applicants respectfully disagree with this conclusion.

Present claim 52 (and hence claims 53-59, 61-63 and 66-68 that depend ultimately therefrom and that are also rejected over Bebee) recites an *in vitro* method for synthesizing one or more nucleic acid molecules comprising one or more site-specific recombination sites, comprising: obtaining at least one isolated linear nucleic acid molecule; contacting the molecule *in vitro* with one or more adapters which comprise at least a first site-specific recombination site or portions thereof under conditions sufficient to add one or more of the adapters to one or more termini of the linear nucleic acid molecule; and mixing the linear nucleic acid molecule with at least one vector, comprising at least a second site-specific recombination site or portions thereof, *in vitro* in the presence of at least one site-specific recombination protein, under conditions sufficient to cause recombination between the first and second site-specific recombination sites, wherein the site-specific recombination protein mediates the recombination.

Present claim 69 (and hence, claim 70 that depends ultimately therefrom and that is also rejected over Bebee) recites an *in vitro* method for synthesizing one or more nucleic acid molecules comprising one or more site-specific recombination sites, comprising: obtaining at least one isolated linear nucleic acid molecule; and contacting the molecule *in vitro* with one or more adapters which comprise at least a first site-specific recombination site or portions thereof under conditions sufficient to add one or more of the adapters to one or more termini of the linear nucleic acid molecule, wherein the at least first site-specific recombination site or portions thereof are *att* sites or mutants or variants thereof.

Present claim 71 (and hence claims 72-74 that depend ultimately therefrom and that are also rejected over Bebee) recites an *in vitro* method for synthesizing one or more nucleic acid molecules comprising two or more site-specific recombination sites, comprising: obtaining at least one isolated linear nucleic acid molecule; and contacting the molecule *in vitro* with two or more adapters which comprise at least a first site-specific recombination site or portions thereof under conditions sufficient to add two or more of the adapters to one or more termini of the linear nucleic acid molecule, wherein the two or more site-specific recombination sites do not recombine with each other.

Present claim 75 (and hence claims 76-78 that depend ultimately therefrom and that are also rejected over Bebee) recites an *in vitro* method for synthesizing one or more nucleic acid molecules comprising two or more site-specific recombination sites, comprising: obtaining at least one isolated linear nucleic acid molecule; and contacting the molecule *in vitro* with one or more adapters which comprise at least a first and second site-specific recombination site or portions thereof under conditions sufficient to add one or more of the

adapters to one or more termini of the linear nucleic acid molecule, wherein the two or more site-specific recombination sites do not recombine with each other.

Under 35 U.S.C. § 102, a claim can only be anticipated if every element in the claim is expressly or inherently disclosed in a single prior art reference. *See Kalman v. Kimberly Clark Corp.*, 713 F.2d 760, 771 (Fed. Cir. 1983), *cert. denied*, 465 U.S. 1026 (1984). Applicants respectfully submit that Bebee does not disclose every element of present claims 52, 69 71 or 75 (and hence the dependent claims noted above), and therefore cannot anticipate the presently claimed invention.

As discussed in the previous reply, filed February 1, 2005 (incorporated by reference herein in its entirety), Applicants respectfully submit that Bebee does not disclose the *in vitro* methods of the presently claimed invention, being limited instead to *in vivo* recombination wherein the recombination takes place inside of host cells. Hence, for at least this reason, Bebee does not anticipate the presently claimed invention.

The Examiner states that "Applicants' assertion that the ordinary meaning of the word 'recombination site' is synonymous with 'site-specific recombination site' is unsupported." Office Action at page 5, third paragraph, lines 1-2. Applicants respectfully disagree, and submit that the ordinarily skilled artisan, guided by the present specification, would readily understand that the terms "recombination site" and "recombination protein" mean that that recombination sites and proteins are site-specific. However, solely to expedite prosecution and not in acquiescence to this rejection, Applicants have revised these terms in the present claims to make explicit that which was at least implicit in the claims as previously presented.

Applicants respectfully submit that Bebee does not disclose all of the elements of the present claim 52, specifically the *in vitro* recombination between the first and second site-specific recombination sites as recited in this claim. Applicants further submit that the Examiner has not provided any reference which discloses all of the elements of present claim 52 (and hence the dependent claims noted above). With regard to present claim 69, Applicants respectfully submit that Bebee does not disclose contacting a nucleic acid molecule *in vitro* with one or more adapters which comprise at least a first site-specific recombination site or portions thereof under conditions sufficient to add one or more of the adapters to the nucleic acid molecule, wherein the at least first site-specific recombination site or portions thereof are *att* sites or mutants or variants thereof. Hence, Bebee does not disclose all of the elements of present claim 69.

Applicants also submit that Bebee does not disclose the *in vitro* methods of claim 71 or claim 75 for synthesizing one or more nucleic acid molecules comprising two or more site-specific recombination sites, using site-specific recombination sites that do not recombine with each other, and hence, Bebee does not disclose every element of these claims.

In responding to Applicants' previous arguments (Office Action at pages 4-6), the Examiner has also stated that "[the] ambiguity as to what is conveyed to the skilled artisan is compounded by the use of terms like 'portion thereof' or 'mutants or variants thereof' in reference to the recombination sites." Office Action at page 6, lines 3-5. Applicants respectfully disagree with the Examiner and submit that the ordinarily skilled artisan, guided by the present specification, would have readily understood the meaning of the terms "portions" and "mutants and variants" as they relate to the site-specific recombination sites.

The Examiner's attention is directed to the present specification at page 28, lines 7-9, where portions of recombination sites are defined as "[p]ortions of recombination sites comprise at least 2 bases, at least 5 bases, at least 10 bases or at least 20 bases of the recombination sites of interest." As discussed above, the ordinarily skilled artisan would have readily understood that the terms "recombination site" and "site-specific recombination site" are interchangeable as used in the present claims and specification. Thus, the ordinarily skilled artisan would have readily understood the meaning of a "portion of a site-specific recombination site." As the present specification discloses numerous representative examples of site-specific recombination sites, "at least 2 bases, at least 5 bases, at least 10 bases, or at least 20 bases" of any of such sites would comprise "portions of site-specific recombination sites."

Finally, with regard to the terms "mutants and variants thereof" Applicants respectfully submit that the present specification discloses numerous examples of mutants and variants of site-specific recombination sites (*see e.g.*, throughout pages 36-46). Thus, the ordinarily skilled artisan would have readily understood the meaning of the terms "mutants and variants thereof" as they relate to site-specific recombination sites.

Therefore, in view of the foregoing remarks, and under *Kalman*, Bebee cannot and does not anticipate the presently claimed invention. Applicants respectfully request reconsideration and withdrawal of the rejection of claims 52-59, 61-63 and 66-78 under 35 U.S.C. § 102(e) over Bebee.

The Rejection Under 35 U.S.C. § 112, Second Paragraph

In the Office Action at pages 6-9, the Examiner has rejected claims 52-69 and 61-78 under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Applicants respectfully traverse this rejection.

The Examiner contends that:

because the terms "recombination site" and "recombination protein" can be interpreted more broadly than what is actually exemplified in the specification, it is not clear from the specification that the terms "recombination site" and "recombination protein" are necessarily limited to site-specific recombinase sites and site-specific recombinases respectively. Therefore, the metes and bounds of what is claimed are unclear.

Office Action at page 7, line 19, through page 8, line 2.

Applicants respectfully disagree, and submit that the ordinarily skilled artisan, guided by the present specification, would have readily understood that the terms "recombination site" and "recombination protein" refer to site-specific recombination sites and recombination proteins, respectively. However, solely to expedite prosecution, and not in acquiescence to this rejection, Applicants have revised these terms in the present claims to make explicit that which was at least implicit in the claims as previously presented.

The Examiner also contends that the nature of the "conditions sufficient to cause recombination of said linear nucleic acid molecule with said vector" recited in claim 52 is unclear. The Examiner further contends that the claim encompasses embodiments wherein the recombination reaction between the vector and linear nucleic acid is not mediated by the recombination protein. Applicants respectfully disagree with these contentions.

Applicants respectfully submit that the ordinarily skilled artisan would readily recognize that the method recited in present claim 52 requires the interaction between the site-specific recombination site(s) on the linear nucleic acid molecule and the site-specific recombination site(s) on the vector, in the presence of a site-specific recombination protein, such that a recombination reaction occurs between the recombination sites mediated by the site-specific recombination protein. Applicants further submit that "conditions sufficient to cause recombination" are well known to those skilled in the art, particularly in view of the significant detailed disclosure of such conditions provided in the present specification (*see e.g.*, Examples 1-12). Applicants therefore respectfully submit that the present specification provides sufficient disclosure of such conditions, and hence, the metes and bounds of these conditions are clearly set forth.

In view of the foregoing remarks, Applicants respectfully request that the rejection of claims 52-59 and 61-78, under 35 U.S.C. § 112, second paragraph, be reconsidered and withdrawn.

The Objection to Claim 64

In the Office Action at page 7, the Examiner has objected to claim 64, indicating that this claim would be free of the cited art if rewritten in independent form comprising each of the limitations of the claim upon which it is currently dependent. Applicants thank the Examiner for identification of this provisionally allowable subject matter. However, in view of the foregoing remarks, Applicants respectfully submit that all of the present claims are allowable. Hence, reconsideration and withdrawal of this objection are respectfully requested.

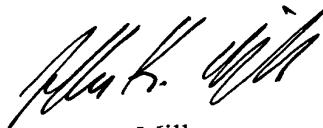
Conclusion

All of the stated grounds of rejection and objection have been properly traversed, rendered moot, or otherwise overcome. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding rejections and objections and that they be withdrawn, and that all pending claims be allowed.

Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.



Jeffrey K. Mills
Agent for Applicants
Registration No. 56,413

Date: July 20, 2005

1100 New York Avenue, N.W.
Washington, D.C. 20005-3934
(202) 371-2600